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Original article

External validation of equations to estimate resting energy expenditure in 14952 adults with overweight and obesity and 1948 adults with normal weight from Italy

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SUMMARY

Background & aims: We cross-validated 28 equations to estimate resting energy expenditure (REE) in a very large sample of adults with overweight or obesity.
Methods: 14952 Caucasian men and women with overweight or obesity and 1498 with normal weight were studied. REE was measured using indirect calorimetry and estimated using two meta-regression equations and 26 other equations. The correct classification fraction (CCF) was defined as the fraction of subjects whose estimated REE was within 10% of measured REE.
Results: The highest CCF was 79%, 80%, 72%, 64%, and 63% in subjects with normal weight, overweight, class 1 obesity, class 2 obesity, and class 3 obesity, respectively. The Henry weight and height and Mifflin equations performed equally well with CCFs of 77% vs. 77% for subjects with normal weight, 80% vs. 80% for those with overweight, 72% vs. 72% for those with class 1 obesity, 64% vs. 63% for those with class 2 obesity, and 61% vs. 60% for those with class 3 obesity. The Sabounchi meta-regression equations offered an improvement over the above equations only for class 3 obesity (63%).
Conclusions: The accuracy of REE equations decreases with increasing values of body mass index. The Henry weight & height and Mifflin equations are similarly accurate and the Sabounchi equations offer an improvement only in subjects with class 3 obesity.

1. Introduction

An evaluation of individual energy expenditure is important to deliver effective weight loss programs. Total energy expenditure (TEE) is most commonly calculated from measured (mREE) or estimated (eREE) resting energy expenditure (REE) using a constant correction for the thermic effect of food and a variable correction for physical activity [1].

As reviewed by Madden et al. [2], REE (kcal$\cdot$day^{-1}) is higher in subjects with than in those without obesity. This is explained by the expansion of fat-free mass (FFM) that accompanies the expansion of fat mass (FM) in most subjects with obesity, with the exception of those with genetic obesities such as the Prader–Willi syndrome [3].

Abbreviations: BMI, body mass index; CCF, correct classification fraction; eREE, estimated resting energy expenditure; FFM, fat-free mass; FM, fat mass; Ht, height; ICANS, International Center for the Assessment of Nutritional Status; IQR, interquartile range; mREE, measured resting energy expenditure; NIH, National Institutes of Health; REE, resting energy expenditure; RQ, respiratory quotient; TEE, total energy expenditure; Wt, weight.

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However, REE standardized on body weight ($kcal \cdot day^{-1} \cdot kg^{-1}$) is lower in obesity because FM, which contributes to REE much less than FFM, accounts for most of the weight of subjects with obesity. Body weight is included in most prediction equations because it explains the greatest portion of REE variability [1]. Mostly because the REE-weight relationship differs in subjects with and without obesity, population-specific equations are considered to be needed for subjects with obesity [2].

Sabounchi et al. [4] have recently developed REE meta-regression equations for 20 population groups by pooling the algorithms produced by 47 studies. The 20 population groups are defined on the basis of race, sex and age and the coefficients of the meta-regression equations are weighted averages of the same coefficients across the available equations for a given population. The attractiveness of the Sabounchi equations lies in the fact that the aggregation of different studies is expected to provide more generalizable estimates. The Sabounchi equations have presently undergone external validation only in a small sample of 30 subjects with values of body mass index (BMI) ranging from 19 to 39 $kg \cdot m^{-2}$ [5].

Madden et al. [2] have recently performed a systematic review of the equations used to estimate REE in adults with overweight and obesity. They evaluated the accuracy of 28 equations that had been cross-validated in external populations. Equations based on simple anthropometric and demographic characteristics were chosen so that they could be easily employed in clinical practice. The conclusion of the systematic review of Madden et al. [2] was that no single equation provided accurate estimates of REE in adults with overweight and obesity.

The aim of the present study was to externally validate the meta-regression equations of Sabounchi et al. [4] and those systematically reviewed by Madden et al. [2] in subjects with overweight or obesity using subjects with normal weight as comparator.

2. Materials and methods

2.1. Study design

We retrospectively collected the data of consecutive Caucasian men and women followed between January 2009 and June 2017 at the International Center for the Assessment of Nutritional Status (ICANS, Milan, Italy) and at the Italian Institute of Auxology (Verbania, Italy). The REE of the subjects with overweight and obesity

Table 1

Measurements of the study subjects. Continuous variables are reported as median (50th percentile) and interquartile range (25th and 75th percentiles). Categorical variables are reported as number and proportion. Abbreviations: BMI = body mass index; eREE = estimated resting energy expenditure; Ht = height; mREE = measured resting energy expenditure; NIH = National Institutes of Health; Wt = weight.

	Women	Men	Total
	N = 12,281	N = 4619	N = 16,900
Center			
Italian Institute of Auxology	5782 (47.1%)	2230 (48.3%)	8012 (47.4%)
International Center for the Assessment of Nutritional Status	6499 (52.9%)	2389 (51.7%)	8888 (52.6%)
Age (years)	48 (37; 57)	48 (38; 57)	48 (37; 57)
Weight (kg)	87 (72; 102)	105 (91; 121)	92 (76; 108)
Height (m)	1.60 (1.55; 1.65)	1.74 (1.70; 1.78)	1.63 (1.57; 1.70)
BMI ($kg \cdot m^{-2}$)	34.0 (27.6; 40.5)	34.8 (30.0; 40.3)	34.3 (28.3; 40.4)
BMI classification (NIH)			
Normal weight	1724 (14.0%)	224 (4.8%)	1948 (11.5%)
Overweight	2595 (21.1%)	929 (20.1%)	3524 (20.9%)
Class 1 obesity	2268 (18.5%)	1196 (25.9%)	3464 (20.5%)
Class 2 obesity	2369 (19.3%)	1060 (22.9%)	3429 (20.3%)
Class 3 obesity	3325 (27.1%)	1210 (26.2%)	4535 (26.8%)
mREE indirect calorimetry ($kcal \cdot day^{-1}$)	1506 (1346; 1711)	1923 (1725; 2200)	1609 (1403; 1865)
mREE indirect calorimetry ($kcal \cdot day^{-1} \cdot kg\ weight^{-1}$)	18 (16; 20)	19 (17; 20)	18 (16; 20)
eREE Bernstein 1983 [14] ($kcal \cdot day^{-1}$)	1279 (1172; 1400)	1618 (1442; 1834)	1344 (1204; 1514)
eREE De Lorenzo 2001 [35] ($kcal \cdot day^{-1}$)	1743 (1561; 1954)	1844 (1686; 2047)	1773 (1595; 1981)
eREE de Luis 2006 [34] ($kcal \cdot day^{-1}$)	1626 (1484; 1798)	1796 (1645; 1986)	1674 (1523; 1854)
eREE Fredrix 1990 [33] ($kcal \cdot day^{-1}$)	1727 (1572; 1916)	2125 (1959; 2332)	1835 (1631; 2067)
eREE Ganpule 2007 [32] ($kcal \cdot day^{-1}$)	1626 (1465; 1814)	2043 (1878; 2251)	1739 (1524; 1970)
eREE Harris 1919 [31] ($kcal \cdot day^{-1}$)	1552 (1416; 1709)	2048 (1843; 2299)	1651 (1464; 1890)
eREE Henry 2005 (Wt) [30] ($kcal \cdot day^{-1}$)	1526 (1379; 1695)	2048 (1848; 2305)	1635 (1431; 1889)
eREE Henry 2005 (Wt & Ht) [30] ($kcal \cdot day^{-1}$)	1488 (1368; 1630)	1979 (1809; 2196)	1582 (1410; 1819)
eREE Huang 2004 [13] ($kcal \cdot day^{-1}$)	1500 (1358; 1660)	1996 (1856; 2175)	1614 (1409; 1866)
eREE Ireton-Jones 1989 [29] ($kcal \cdot day^{-1}$)	1878 (1654; 2140)	2262 (2004; 2595)	1971 (1717; 2285)
eREE Kleiber 1932 [28] ($kcal \cdot day^{-1}$)	1538 (1403; 1699)	1806 (1652; 1999)	1610 (1446; 1802)
eREE Korth 2007 [27] ($kcal \cdot day^{-1}$)	1561 (1418; 1731)	2121 (1967; 2311)	1681 (1473; 1970)
eREE Livingston 2005 [26] ($kcal \cdot day^{-1}$)	1482 (1352; 1623)	1503 (1385; 1642)	1488 (1361; 1628)
eREE Mifflin 1990 [25] ($kcal \cdot day^{-1}$)	1465 (1322; 1635)	1898 (1744; 2086)	1573 (1375; 1803)
eREE Muller 2004 [24] ($kcal \cdot day^{-1}$)	1572 (1409; 1752)	2015 (1857; 2214)	1691 (1468; 1918)
eREE Muller 2004 (BMI) [24] ($kcal \cdot day^{-1}$) [a]	1604 (1461; 1774)	2042 (1881; 2253)	1725 (1517; 1959)
eREE Owen 1986; 1987 [23,36] ($kcal \cdot day^{-1}$)	1417 (1310; 1528)	1948 (1805; 2114)	1499 (1349; 1745)
eREE Roza 1984 [22] ($kcal \cdot day^{-1}$)	1533 (1402; 1687)	2050 (1854; 2294)	1633 (1449; 1879)
eREE Schofield 1985 (Wt) [21] ($kcal \cdot day^{-1}$)	1539 (1411; 1688)	2039 (1857; 2262)	1634 (1456; 1888)
eREE Schofield 1985 (Wt & Ht) [21] ($kcal \cdot day^{-1}$)	1550 (1414; 1705)	2029 (1842; 2259)	1646 (1460; 1908)
eREE Siervo 2003 [20] ($kcal \cdot day^{-1}$)	1539 (1367; 1716)	1747 (1586; 1935)	1600 (1418; 1784)
eREE Tabata 2012 [18] ($kcal \cdot day^{-1}$)	1863 (1542; 2194)	2253 (1952; 2604)	1978 (1638; 2321)
eREE Weijs 2010 [19] ($kcal \cdot day^{-1}$)	1663 (1462; 1886)	2119 (1922; 2360)	1790 (1533; 2049)
eREE WHO 1985 (Wt) [17] ($kcal \cdot day^{-1}$)	1579 (1440; 1734)	2068 (1888; 2286)	1678 (1488; 1927)
eREE WHO 1985 (Wt & Ht) [17] ($kcal \cdot day^{-1}$)	1568 (1435; 1723)	2062 (1873; 2290)	1665 (1480; 1910)
eREE Sabounchi (S1) 2013 [4] ($kcal \cdot day^{-1}$)	1528 (1383; 1692)	2012 (1867; 2200)	1643 (1435; 1889)

[a] Not available for the 1948 subjects with normal weight.

was measured at the inception of a weight-loss program at both Centers. The REE of the subjects with normal weight was measured only at ICANS, which offers weight-maintaining and nutrition counseling programs also for subjects with normal weight. The inclusion criteria were: 1) age ≥18 years; 2) BMI ≥18.5 kg·m^{-2} and; 3) availability of REE. The exclusion criteria were: 1) syndromic obesity [6]; 2) dysthyroidism; 3) use of drugs known to affect energy expenditure (e.g. levothyroxine) and; 4) respiratory quotient (RQ) <0.67 or >1.3 [7]. The study protocol was approved by the Ethical Committee of the Italian Institute of Auxology.

2.2. Anthropometric assessment

Weight and height were measured following international guidelines [8]. BMI was calculated as weight (kg)·height (m)$^{-2}$ and classified as normal weight (18.5 ≤ BMI ≤ 24.9 kg·m^{-2}), overweight (25.0 ≤ BMI ≤ 29.9 kg·m^{-2}), class 1 obesity (30.0 ≤ BMI ≤ 34.9 kg·m^{-2}), class 2 obesity (35.0 ≤ BMI ≤ 39.9 kg·m^{-2}), and class 3 obesity (BMI ≥ 40.0 kg·m^{-2}) [9].

2.3. REE measurement

In both study centers, REE was measured between 8:00 and 10:00 AM in thermo-neutral conditions using an open-circuit indirect calorimeter equipped with a canopy (Vmax 29, Sensor Medics, Yorba Linda, CA). Each indirect calorimeter underwent an ethanol burning test at least one time per year during the study period. The gas analyzers were calibrated before each test using a reference gas mixture made of 15% O_2 and 5% CO_2. The subjects were in the fasting state from at least 8 h, were not smoking from at least 1 h, and waited at least 30 min in the sitting position before undergoing REE measurement. REE was measured in the supine position for at least 30 min, including an acclimation period of 10 min. The data relative to the acclimation period were discarded. The steady state was defined as at least 5 min with less than 5% variation in RQ, less than 10% variation in O_2 consumption, and less than 10% variation in minute ventilation [7]. After the steady state was reached, O_2 consumption and CO_2 production were recorded at intervals of 1 min for at least 20 min and averaged over the whole measurement period. REE was calculated from O_2 consumption and CO_2 production using Weir's equation [10].

2.4. REE estimation

REE was estimated using 2 of the 20 Sabounchi meta-regression equations [4] and 26 of the 28 equations systematically reviewed by Madden [2].

The two Sabounchi equations employed for the present study are the so-called S1 equations: 1) REE (kcal·day^{-1}) = 10.2·weight (kg) + 3.09·height (cm) - 3.09·age (years) + 301 for women and, 2) REE (kcal·day^{-1}) = 10.4·weight (kg) + 3.19·height (cm) - 3.10·age (years) + 522 for men. These are the Sabounchi weight and height equations applicable to white men and women aged ≥18 years and thus to our study subjects [4]. Although the equations contributing the most weight to the Sabounchi meta-regression equations were developed at the Italian Institute of Auxology (on a sample of subjects different from that enrolled for the present study) [11], other algorithms were taken into account by the Sabounchi equations [12–14]. Moreover, 53% of the present subjects were enrolled at ICANS, which was not involved in the development of the Italian Institute of Auxology REE equations [11]. Thus, we considered the Sabounchi equations suitable for our purpose of externally validating REE equations.

Two of the 28 equations reviewed by Madden et al. [2] had been developed at the Italian Institute of Auxology (on a sample of subjects different from that enrolled for the present study) and were therefore not considered suitable for the present study aimed at validating externally developed equations [15,16]. All the remaining 26 equations [13,14,17–36] were evaluated in the present study.

Table 2
Percent bias of the REE equations. Variables are reported as median (50th percentile) and interquartile range (25th and 75th percentiles).

	Normal weight	Overweight	Class 1 obesity	Class 2 obesity	Class 3 obesity
	N = 1948	N = 3524	N = 3464	N = 3429	N = 4535
Bernstein 1983 [14]	−14 (−19;−9)	−15 (−19;−10)	−16 (−21;−10)	−16 (−22;-10)	−17 (−23;−11)
De Lorenzo 2001 [35]	13 (6; 19)	11 (2;19)	9 (−1; 19)	10 (−2; 20)	11 (−1; 21)
de Luis 2006 [34]	9 (3;17)	6 (−2; 13)	3 (−6; 11)	2 (−7; 12)	2 (−7; 11)
Fredrix 1990 [33]	17 (11;24)	15 (9;21)	13 (6;21)	12 (3;20)	11 (2;19)
Ganpule 2007 [32]	7 (1;13)	8 (2;13)	8 (1;14)	7 (−1; 14)	6 (−2; 15)
Harris 1919 [31]	4 (−1; 10)	4 (−1; 10)	4 (−2; 10)	3 (−4; 11)	2 (−6; 10)
Henry 2005 (Wt) [30]	1 (−5; 6)	2 (−3; 8)	3 (−3; 10)	3 (−5; 11)	2 (−6; 11)
Henry 2005 (Wt & Ht) [30]	2 (−4; 8)	1 (−4; 7)	1 (−5; 7)	−1 (−8; 6)	−3 (−11; 5)
Huang 2004 [13]	0 (−6; 6)	1 (−4; 7)	1 (−5; 8)	0 (−7; 7)	−1 (−9; 6)
Ireton-Jones 1989 [29]	31 (22; 39)	37 (29; 46)	5 (−4; 15)	15 (4;26)	26 (15; 40)
Kleiber 1932 [28]	5 (−1; 11)	3 (−3; 9)	0 (−7; 7)	−2 (−10; 7)	−5 (−13; 4)
Korth 2007 [27]	7 (1;14)	7 (1;13)	6 (0; 13)	4 (−4; 12)	2 (−6; 10)
Livingston 2005 [26]	−2 (−9; 4)	−4 (−14; 2)	−7 (−19; 1)	−8 (−20; 1)	−10 (−20;-1)
Mifflin 1990 [25]	−1 (−7; 4)	−1 (−7; 4)	−2 (−8; 4)	−3 (−11; 4)	−4 (−12; 3)
Muller 2004 [24]	2 (−3; 8)	4 (−1; 9)	5 (−1; 11)	4 (−3; 11)	4 (−4; 12)
Muller 2004 (BMI) [24]	Not available	4 (−1; 9)	3 (−3; 10)	4 (−4; 11)	4 (−4; 12)
Owen 1986; 1987 [23,36]	−4 (−9; 3)	−2 (−8; 4)	−3 (−9; 4)	−6 (−13; 2)	−8 (−15; 0)
Roza 1984 [22]	4 (−2; 10)	4 (−2; 9)	3 (−3; 10)	2 (−5; 9)	1 (−7; 9)
Schofield 1985 (Wt) [21]	4 (−1; 10)	5 (−1; 10)	4 (−3; 11)	2 (−6; 11)	1 (−7; 10)
Schofield 1985 (Wt & Ht) [21]	7 (0; 15)	6 (−1; 12)	4 (−3; 11)	2 (−6; 11)	0 (−8; 9)
Siervo 2003 [20]	−4 (−10; 2)	−3 (−9; 4)	−2 (−9; 5)	−1 (−10; 7)	0 (−9; 9)
Tabata 2012 [18]	1 (−5; 8)	11 (5;18)	19 (11;27)	25 (15;35)	33 (22; 44)
Weijs 2010 [19]	3 (−2; 9)	8 (2;14)	10 (4;17)	11 (3;19)	12 (4;21)
WHO 1985 (Wt) [17]	6 (0; 12)	6 (1;12)	6 (−1; 13)	5 (−3; 13)	4 (−4; 12)
WHO 1985 (Wt & Ht) [17]	6 (0; 12)	7 (1;12)	5 (−1; 13)	4 (−4; 12)	2 (−6; 11)
Sabounchi (S1) 2013 [4]	2 (−4; 7)	3 (−2; 8)	3 (−3; 9)	1 (−6; 9)	0 (−7; 8)

2.5. Statistical analysis

Most continuous variables were not Gaussian-distributed and all are reported as median (50th percentile) and interquartile range (IQR, 25th and 75th percentiles). Categorical variables are reported as the number and proportion of subjects with the characteristic of interest. Bland–Altman plots of the absolute bias (eREE - mREE) vs. the average bias [(eREE + mREE)/2] and of the percent bias [(eREE − mREE)/mREE] vs. the average bias were used to investigate the presence of proportional bias [37]. The correct classification fraction (CCF) of an equation was defined as the fraction of subjects whose eREE was within 10% of mREE [2]. Not unexpectedly [37], proportional bias was detected for almost all equations using both absolute and percent bias (data not shown). Because of this fact and

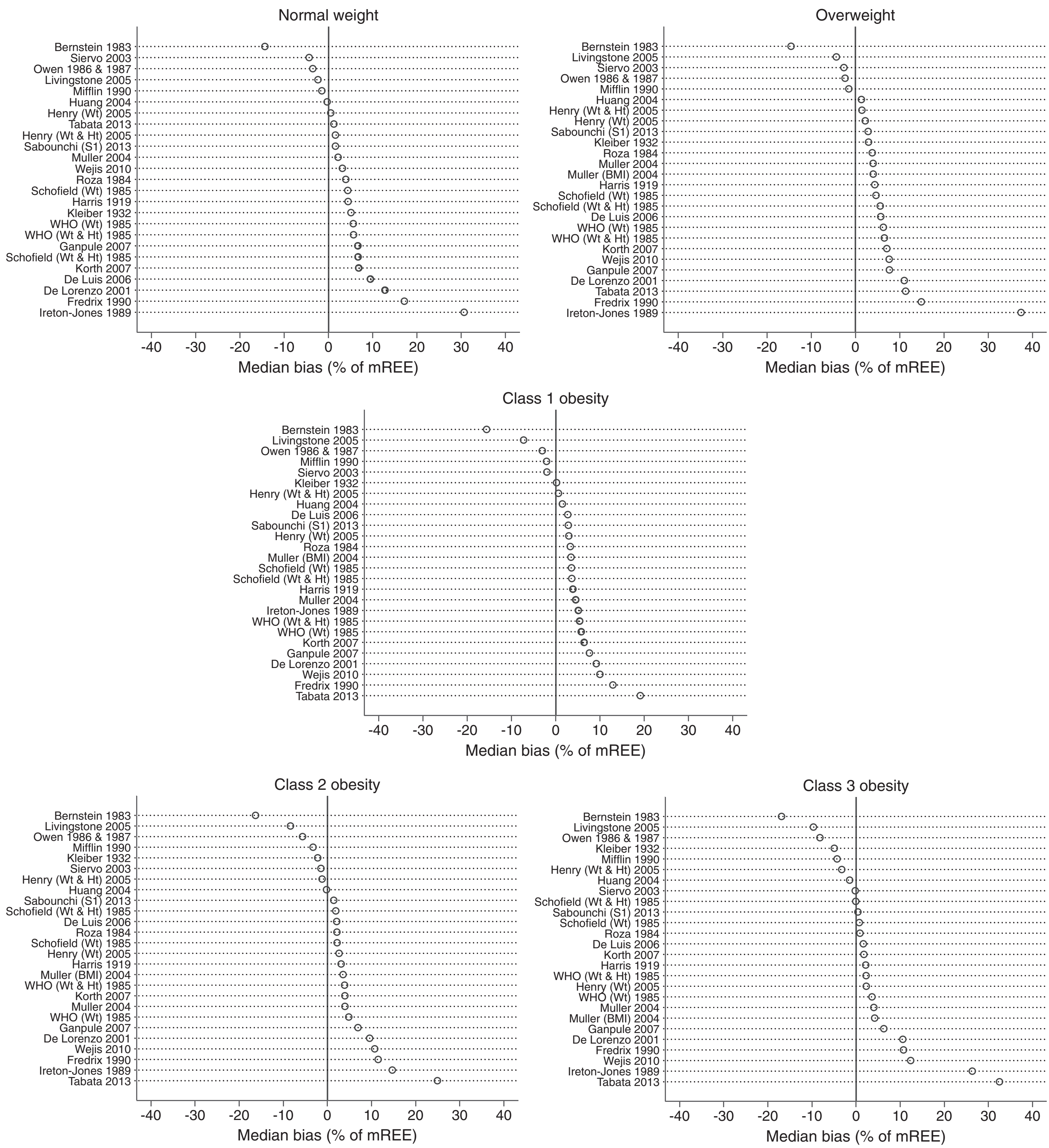

Fig. 1. Dot chart showing the median percent bias of the REE equations. The best equation is that with the dot nearest to the 0 value of the Y-axis.

of our primary interest in the CCF of the equations [2], the Bland–Altman limits of agreement were not computed [37]. Statistical analysis was performed using Stata 14.2 (Stata Corporation, College Station, TX, USA).

3. Results

Table 1 gives the anthropometric measurements, the mREE and the eREEs of the 16,900 studied subjects.

The median (IQR) age of the subjects was 48 (37; 57) years and 72.7% of them were women (Table 1). 11.5% of the subjects had a normal weight, 20.9% were overweight, 20.5% had class 1 obesity, 20.3% had class 2 obesity, and 26.8% had class 3 obesity (Table 1).

Table 2 gives the median (IQR) percent bias of the REE equations stratified by BMI class. Using this criterion, the best equation is that with the median bias nearest to 0 and the narrowest IQR.

The median percent bias of the REE equations is also plotted in Fig. 1. Using this criterion, the best equation is that with the dot nearest to the 0 value of the Y-axis.

Table 3 gives the CCF, i.e. the proportion of subjects whose eREE was within 10% of mREE. Using this criterion, the best equation is that with the highest CCF. This criterion is more useful than the median (IQR) bias to evaluate the applicability of the REE equations at the individual level [2].

The CCF is also plotted in Fig. 2. According to this criterion, the best equation is that with the dot corresponding to the highest value on the Y-axis. Looking at Fig. 2, it can be clearly seen that, moving from subjects with normal weight to those with class 3 obesity, the CCF of all equations decreases substantially (from 79% to 63% under the best case scenario).

Among the subjects with normal weight, the highest CCF was associated with the Henry weight (Wt) equation (79%, 95% confidence interval 77–81%) followed by the Huang (78%, 76%–80%), Sabounchi (78%, 76%–80%), and Mifflin equation (77%, 76%–79%) (Table 3 and Fig. 2).

Among the subjects with overweight, the highest CCF was associated with the Henry weight and height (Wt & Ht) (80%, 95% confidence interval 78%–81%) and the Mifflin equation (80%, 78%–81%) followed by the Huang (78%, 77%–80%), Henry Wt (78%, 76%–79%), and Sabounchi equation (77%, 76%–79%) (Table 3 and Fig. 2).

Among the subjects with class 1 obesity, the highest CCF was associated with the Mifflin equation (72%, 95% confidence interval 71%–74%) and the Henry Wt & ht equation (72%, 71% to 74), followed by the Huang (71%, 69%–72%), and Sabounchi (70%, 69–72%) equations (Table 3 and Fig. 2).

Among the subjects with class 2 obesity, the highest CCF was associated with the Huang equation (65%, 95% confidence interval 64%–67%) followed by the Sabounchi (64%, 63%–66%), Henry Wt & ht (64%, 62–66%), and Mifflin equation (63%, 61%–65%) (Table 3 and Fig. 2).

Lastly, among the subjects with class 3 obesity, the highest CCF was associated with the Huang equation (63%, 95% confidence interval 62–65%), followed by the Sabounchi (63%, 61–64%), Roza (61%, 59–62%), Henry Wt & ht (61%, 59–62%), and Mifflin (60%, 59–61%) equations (Table 3 and Fig. 2).

4. Discussion

In the largest study performed so far on Caucasian adults with overweight and obesity, we evaluated the accuracy of two of the 20 REE meta-regression equations of Sabounchi et al. [4] and 26 [13,14,17–36] of the 28 REE equations systematically reviewed by Madden et al. [2].

In agreement with Madden et al. [2], we found that the Henry Wt & Ht and the Mifflin equations gave similarly accurate predictions of REE. The CCFs for the Mifflin and the WHO equations were better than those obtained in a previous study performed at the Italian Institute of Auxology [11]. The greater accuracy of the WHO and Mifflin equations in the present study may be partly explained by a different case-mix of subjects. 53% of the subjects

Table 3
Correct classification fraction of the REE equations, i.e. proportion of subjects whose estimated resting energy expenditure was within 10% of measured resting energy expenditure.

	Normal weight	Overweight	Class 1 obesity	Class 2 obesity	Class 3 obesity
	N = 1948	N = 3524	N = 3464	N = 3429	N = 4535
Bernstein 1983 [14]	28%	24%	25%	24%	23%
De Lorenzo 2001 [35]	36%	42%	43%	39%	38%
de Luis 2006 [34]	49%	58%	57%	53%	54%
Fredrix 1990 [33]	23%	30%	37%	41%	43%
Ganpule 2007 [32]	64%	61%	56%	53%	53%
Harris 1919 [31]	72%	73%	67%	61%	60%
Henry 2005 (Wt) [30]	79%	78%	68%	60%	58%
Henry 2005 (Wt & Ht) [30]	77%	80%	72%	64%	61%
Huang 2004 [13]	78%	78%	71%	65%	63%
Ireton-Jones 1989 [29]	5%	1%	52%	34%	16%
Kleiber 1932 [28]	68%	72%	66%	58%	54%
Korth 2007 [27]	61%	60%	58%	59%	60%
Livingston 2005 [26]	72%	62%	50%	47%	45%
Mifflin 1990 [25]	77%	80%	72%	63%	60%
Muller 2004 [24]	78%	75%	66%	60%	59%
Muller 2004 (BMI) [24]	Not available	75%	69%	61%	58%
Owen 1986; 1987 [23,36]	71%	72%	66%	55%	50%
Roza 1984 [22]	74%	76%	69%	63%	61%
Schofield 1985 (Wt) [21]	71%	71%	65%	59%	58%
Schofield 1985 (Wt & Ht) [21]	60%	65%	62%	57%	56%
Siervo 2003 [20]	69%	69%	64%	58%	56%
Tabata 2012 [18]	71%	45%	21%	15%	8%
Weijs 2010 [19]	72%	60%	48%	43%	39%
WHO 1985 (Wt) [17]	68%	65%	61%	56%	56%
WHO 1985 (Wt & Ht) [17]	66%	64%	61%	57%	58%
Sabounchi (S1) 2013 [4]	78%	77%	70%	64%	63%

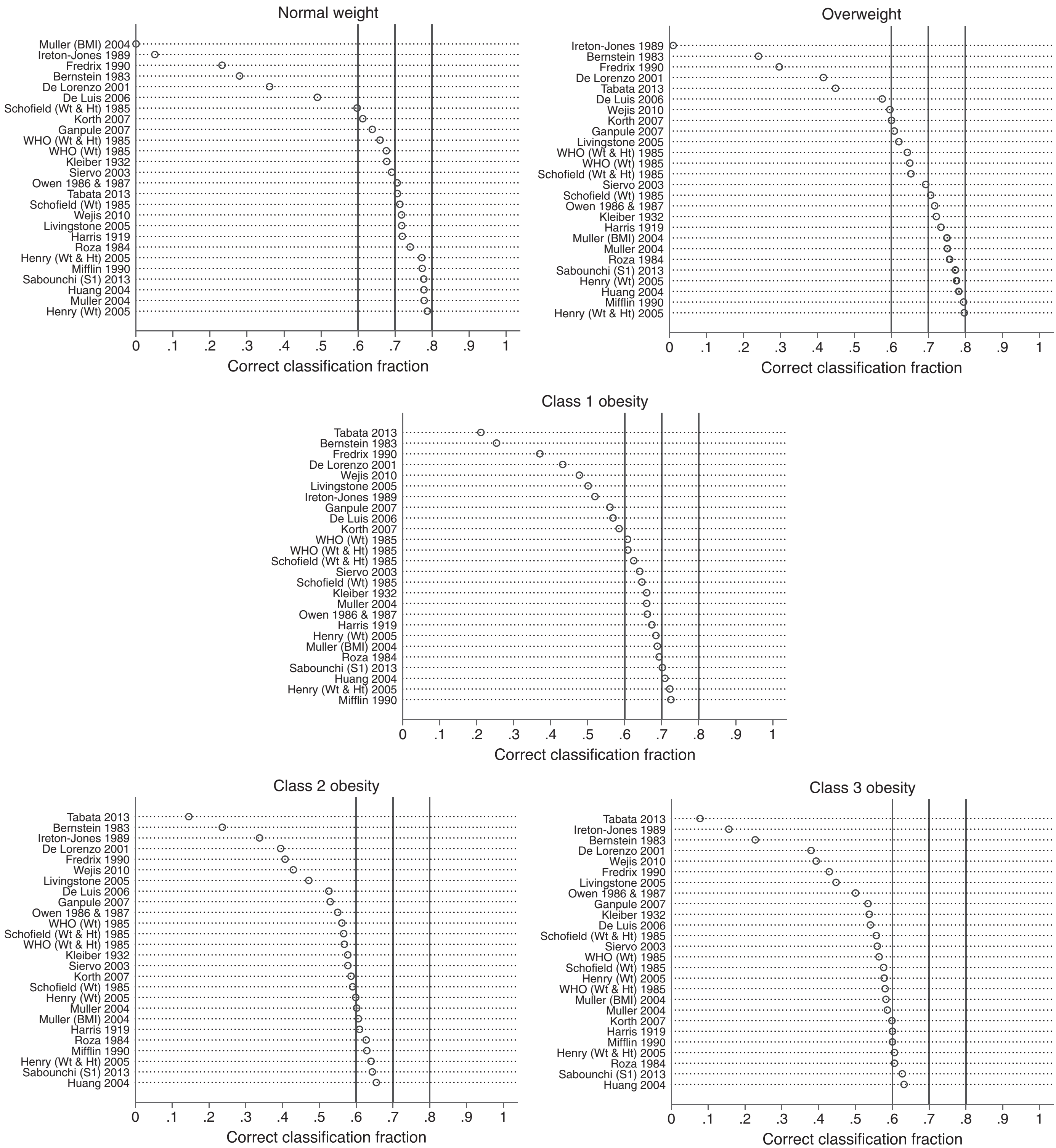

Fig. 2. Dot chart showing the correct classification fraction of the REE equations. The best equation is that with the dot corresponding to the highest value on the Y-axis.

were in fact contributed by ICANS and the remaining 47% were not involved in the previous study performed at the Italian Institute of Auxology [11]. The Sabounchi equation performed better than the Henry Wt & Ht and Mifflin equations only in subjects with class 3 obesity. The Sabounchi equation was however paralleled by the Huang equation, which showed also similar or slightly better CCFs for subjects with normal-weight, overweight, class 1 and class 2 obesity. (It is to be noted that the Huang equation is one of those used by Sabounchi to develop the meta-regression equations). It is noteworthy that there was not a clear winner among the REE equations within any given BMI class (Table 3) and that an equation developed in the general population, i.e. the Henry Wt & Ht equation, had the same accuracy of one specifically developed in obese subjects, i.e. the Mifflin equation (Table 3).

The main strength of the present study is the very large number of enrolled subjects (N = 19,600) and their balanced distribution within the classes of overweight (N = 3524), degree 1 obesity (N = 3464), degree 2 obesity (N = 3429), and degree 3 obesity (N = 4535). Another strength of the present study is that REE was measured using the same instrumentation and protocol at the two study Centers. This is expected to reduce the variability of the bias attributable to the application of the reference method, i.e. indirect calorimetry. Another strength of the present study is the use of a comparator group of subjects with normal weight (N = 1948). We believe that the present study adds substantially to the available data, which were collected mostly on subjects with overweight or class 1 obesity [2].

The present study has nonetheless two clear limitations. The first limitation is that we studied only Caucasian subjects. Non-Caucasian individuals account for less than 2% of the subjects presently followed at our Centers. The number of non-Caucasian subjects available during the time frame of the study was too low to allow a precise estimate of the bias of the REE equations, especially because stratification on BMI was needed (Tables 2 and 3) [2]. The second limitation is that our findings may not extend to the general population. This is possibly true also for the subjects with normal weight, because the fact that they sought professional help to maintain their weight and/or ameliorate their diet is likely to select an health-conscious sector of the population. However, if one considers the 50th (34.3 $kg \cdot m^{-2}$) and 75th (40.3 $kg \cdot m^{-2}$) percentiles of BMI of our study subjects, it should be clear that subjects with such degree of obesity can be adequately studied only at specialized centers such as ICANS and the Italian Institute of Auxology.

The very high number of studied subjects allowed us to obtain precise estimates of the CCF. Because of such precision, we can confidently state that, in our study sample, the Henry Wt & Ht and Mifflin equations perform equally well with a CCF of 77% vs. 77% among subjects with normal weight, 80% vs. 80% among subjects with overweight, 72% vs. 72% among subjects with class 1 obesity, 64% vs. 63% among subjects with class 2 obesity, and 60% vs. 60% among subjects with class 3 obesity and that the Sabounchi equations offers an improvement over these equations only in class 3 obesity (CCF = 63%).

The most interesting finding of the present study is that, if one chooses the most accurate equation for a given BMI class, the CCF decreases from 79% among subjects with normal weight and 80% among subjects with overweight to 72% among subjects with class 1 obesity to 64% among subjects with class 2 obesity to 63% among subjects with class 3 obesity (Table 3 and Fig. 2). Thus, the accuracy of REE equations decreases substantially with increasing BMI. This has important practical implications as the higher is the BMI of the subject, the higher is the possibility of having her/his REE misclassified with the currently employed REE equations independently of the fact that they were developed in overweight and obese subjects.

In conclusion, the accuracy of REE equations decreases with increasing BMI. The Henry Wt & Ht and Mifflin equations are similarly accurate to estimate the REE of subjects with overweight and obesity. The Sabounchi equations are more accurate than these equations only in subjects with class 3 obesity.

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Authors' contributions

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Conflicts of interest

The authors declare that they have no conflict of interest.

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